Modulators of human peroxisome proliferator-activated receptor (hPPAR) from selected medicinal plants have potential use in the prevention and/or treatment of insulin resistance

Christensen, Kathrine Bisgaard; Petersen, Rasmus Koefoed; Jørgensen, Monica; Kotowska, Dorota Ewa; Kristiansen, Karsten; Christensen, Lars Porskjær

Publication date:
2009

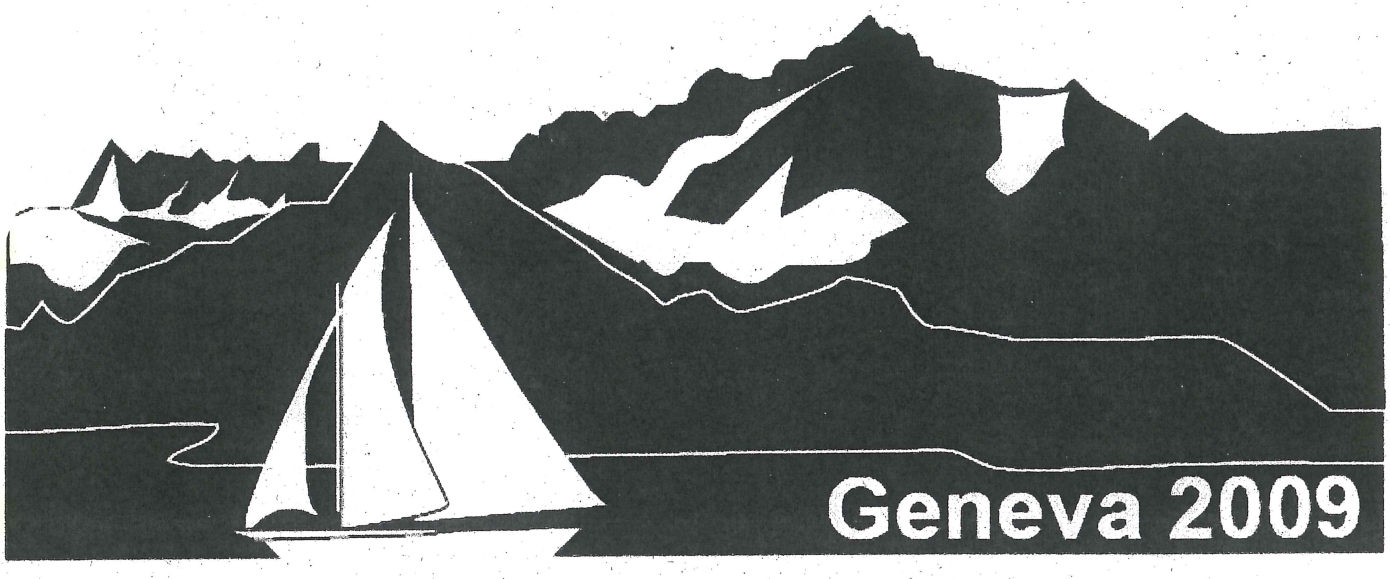
Document version
Final published version

Citation for pulished version (APA):
Christensen, K. B., Petersen, R. K., Jørgensen, M., Kotowska, D. E., Kristiansen, K., & Christensen, L. P. (2009). Modulators of human peroxisome proliferator-activated receptor (hPPAR) from selected medicinal plants have potential use in the prevention and/or treatment of insulin resistance. Abstract from 57th International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research, Geneve, Switzerland.

UNIVERSITÉ DE GENÈVE

G A

Ecole de Pharmacie
EPGL
Genève – Lausanne



57th International Congress & Annual Meeting of the
Society for Medicinal Plant and Natural Product Research

Book of abstracts
Addendum

GENEVA, SWITZERLAND
16th to 20th August 2009

diterpene concentrations for plant development stage during the growing season were found. **References**: [1] Poeckel, D. et al. (2008) Biochemical Pharmacology 76, 91-97. [2] Kavvadias, M. et al. (2003) Planta Med. 69, 113-117.

PH51

Modulators of human peroxisome proliferator-activated receptor γ (hPPARγ) from selected medicinal plants have potential use in the prevention and/or treatment of insulin resistance

Christensen KB[1], Petersen RK[2], Jørgensen M[1], Kotowska D[3], Kristiansen K[4], Christensen LP[1].

[1] Inst. Chemical Engineering, Biotechnology and Environmental Technology, University of Southern Denmark (SDU), Niels Bohrs Allé 1,5230 Odense M, Denmark; [2] BioLigands ApS, International Science Park Odense, 5230 Odense M, Denmark; [3] Dept. Biochemistry and Molecular Biology, SDU, Campusvej 55, 5230 Odense M, Denmark; [4] Dept. Biology, University of Copenhagen, Ole Maaløes Vej 5,2200 Copenhagen N, Denmark

The metabolic syndrome constitutes a set of metabolic risk factors that predisposes individuals to a number of diseases such as type 2 diabetes (T2D). Insulin resistance (IR) is one of these metabolic risk factors that can lead to the development of T2D. IR can be treated with insulin sensitizing drugs such as thiazolidinediones, which are full agonists of PPARγ, and hence may induce severe side effects. Partial PPARγ agonists maintain the beneficial effect on IR without inducing severe side effects. Recently, a general screening for potential partial PPARγ agonists was carried out on several plant extracts. The most active extracts were those of elderflower (*Sambucus nigra*), purple coneflower (*Echinacea purpurea*), sage (*Salvia officinalis*), and buckwheat (*Fagopyrum tataricum*) [1]. Active metabolites were isolated by bioassay-guided fractionation using a PPARγ transactivation assay. Fatty acids (FAs) such as linoleic and α-linolenic acid were identified as PPARγ agonists from all investigated plant extracts. Alkamides are structurally similar to FAs and a new alkamide, hexadeca-2*E*,9*Z*,12*Z*,14*E*-tetraenoic acid isobutylamide, isolated from purple coneflower was able to activate PPARγ and stimulate glucose uptake in adipocytes [2]. Polyphenols are widespread in both elderflowers and buckwheat but only naringenin was able to activate PPARγ [3]. From sage the diterpene 12-*O*-methylcarnosic acid was found to activate PPARγ. The present data suggests that common FAs are responsible for the PPARγ activity of plant extracts together with specific groups of secondary metabolites such as alkamides and flavonoid aglycones, whereas phenolic acids and flavonoid glycosides are not PPARγ agonists. The present investigations also show that plants contain compounds, which can be used in the management of IR and T2D. **References**: [1] Christensen KB et al. (2009) Phytother. Res. in press. [2] Christensen KB et al. (2009) J. Nat. Prod. 72:933–937. [3] Christensen KB et al. (2009) Phytother. Res. accepted.

PH52

An extract from purslane herb might modulate glucose metabolism through multiple mechanisms

Perrinjaquet-Moccetti T, Schellekens C, Verbruggen M

Frutarom Switzerland Ltd, Medical Sciences Pharma Division, Rütiwisstrasse 7, 8820 Wädenswil, Switzerland

The purslane herb (*Portulaca oleracea* L.) is a very common plant used worldwide as a food ingredient. It is traditionally used in folk medicine for a variety of ailments, in Near East purslane is treasured as an aid against diabetes. Animal studies confirm that purslane herb has antidiabetic properties [1-3].

To investigate the efficacy of the herb for this indication, a hydroalcoholic extract from purslane herb, Portusana™ (EFLA®308), was tested *in vitro* in three different assays related to glucose metabolism. Firstly, a glucose rapid-uptake assay was performed in Caco-2 cells to model glucose uptake through the intestinal wall. The extract significantly decreased the absorption of glucose compared to the control. Reduced glucose absorption through the intestine may contribute to a hypoglycaemic effect. Secondly, to assess whether the extract could affect glucose disposal in metabolically active cells, a glucose uptake assay was conducted in differentiated 3T3-L1 adipocytes as a model for adipose tissue. Portusana dose-dependently stimulated the uptake of glucose, both in presence and absence of insulin. These results show that the extract may enhance glucose disposal in adipocytes. Thirdly, the ability to modulate the nuclear receptor PPARγ was investigated in HEC-1B cells, since PPARγ is an important molecular target for antidiabetic activity. Portusana showed agonistic as well as antagonistic activity on PPARγ, clearly suggesting that the constituents in the extract are able to bind and to activate PPARγ. In conclusion, the findings from these *in vitro* studies suggest that Portusana™ may affect different mechanisms related to the pathophysiology of diabetes mellitus. **References**: [1] Eskander, E.F., Won Jun, H. (1995) Egypt. J. Pharm. Sci 36, 1-6: 331-342. [2]. Shen, L., Lu, F. (2003) CJIM 9:289-292. [3] Sinha B.P. et al. (1962) Seyler's Zeit: 274-275.

PH53

Antioxidant effect of *Ziziphus vulgaris*, *Portulaca oleracea*, *Berberis integerima* and *Gundelia tournefortti*

Eshraghi A[1], Asgari S[2], Movahedian Ataar A[1], Naderi GhA[2], Badiee A[1]

[1] School of Pharmacy, Isfahan University of Medical Science, P.O.Box: 81745-359, IR. Iran; [2] Isfahan Cardiovascular Research Center,8146-1148, Isfahan University of Medical Science, IR, Iran

Free radicals especially reactive oxygen species can produce some disorders by damaging biomolecules like Deoxyribonucleic Acid (DNA), proteins, and membrane lipids. Lipid peroxidation in Low-Density Lipoprotein (LDL) and membranes of hepatocytes are involved in atherosclerosis and liver disease respectively. Non-enzymatic glycosylation of proteins is involved in complications of diabetes. We studied the antioxidant effects of some plants, namely, *Ziziphus vulgaris*, *Portulaca oleracea*, *Berberis integerima*, *Gundelia tournefortti* on the above mentioned reactions. Ethanolic and water extracts of the mentioned plants were prepared in three different concentrations:2.5, 5 and 10 µg/ml. Hepatocytes of rat were exposed to tert-butyl hydroperoxide (TBH). The amount of Alanine Aspartate Aminotransferase (AST) released from membrane lipid peroxidation was also measured in presence and absence of the plant extract. Glycosylation. The changes of hemoglobin and red blood cell hemolysis were measured in the presence and absence of the extract. The percent of oxidation inhibition was compared with that in control subjects. Tukey test was used and significance determined at $p<0.001$.The results showed the highest extent of glycosylation inhibition of hemoglobin was due to Gundelia and Berberis by 33.33% and 28.3% respectively. Portulaca, Gundelia and Berberis decreased AST release from hepatocytes by 69.7% and 45% and 59% respectively and Berberis decreased AST release from hepatocytes by 64%. The highest extent of hemolysis inhibition of red blood cell was due to Ziziphus, Gundelia and Berberis by 67%, 56% and 43% respectively. This study showed that the plants have an antioxidant effect and they can be probably used as an antioxidant in food supplement in diabetic and liver disease patients.

Topic I Cosmetics, flavours and aromas

PI42

Volatile compounds of three *Thymus sipyleus* subspecies from different sites in Turkey

Duymus HG[1], Kurkcuoglu M[1], Baser KHC[1], Turgut K[2]

[1] Anadolu University, Faculty of Pharmacy, Department of Pharmacognosy, 26470 Eskisehir, Turkey; [2] Akdeniz University, Faculty of Agriculture, Antalya, Turkey

The genus Thymus (Lamiaceae) is represented by 38 species and 64 taxa, 20 of which are endemic in Turkey. Volatile compounds isolated by microdistillation from nine samples of *Thymus sipyleus* Boiss. subsp. *sipyleus* var. *sipyleus*, *T. sipyleus* Boiss. subsp. sipyleus Boiss. var. davisianus Ronniger, and *T. sipyleus* Boiss. subsp. *rosulans* (Borbas) Jalas were analysed by GC and GC/MS. *T. sipyleus* subsp. *sipyleus* var. *sipyleus* was collected from 3 regions in Elmali, Antalya. 1,8-Cineole (11.2%) and p-cymene (21.8%), α-terpineol (38.6%) and carvacrol (20.5%), 1,8-cineole (11.6%) and carvacrol (18.2%) were identified as major compounds in three samples respectively. *T. sipyleus subsp. sipyleus var. davisianus* was collected from *3* regions in Saklikent, Antalya. Geranial (30.3%) and neral (19.6%), 1,8-cineole (31.1%) and β-caryophyllene (14.6%), and α-terpineol (19.8%) and geranial (11.1%) were the main compounds in the samples respectively. *T. sipyleus subsp. rosulans* was collected from 3 regions in Gazipaşa, Antalya. β-Caryophyllene (14.2%) and intermedeol (13.2%), 1,8-cineole (11.6%) and α-terpineol (35.4%), α-pinene (18.4%) and β-caryophyllene (8.9%) were the major compounds of the samples respectively. Thymol is the main compound in most *Thymus* species in Turkey. According to our study, chemical polymorphisms have been found among the *T. sipyleus* subspecies.

PI43

Essential oil composition of *Matricaria chamomilla* var. *chamomilla* and var. *recutita* from Turkey

Mine Kürkcüoğlu[1], Hüseyin İnceer[2], Sema Ayaz[2], K. Hüsnü Can Başer[1]